FGF23 gene

fibroblast growth factor 23

Normal Function

The *FGF23* gene provides instructions for making a protein called fibroblast growth factor 23, which is produced in bone cells. This protein is necessary in regulating the phosphate levels within the body (phosphate homeostasis). Among its many functions, phosphate plays a critical role in the formation and growth of bones in childhood and helps maintain bone strength in adults. Phosphate levels are controlled in large part by the kidneys. The kidneys normally rid the body of excess phosphate by excreting it in urine, and they reabsorb this mineral into the bloodstream when more is needed. Fibroblast growth factor 23 signals the kidneys to stop reabsorbing phosphate into the bloodstream.

In order to function, fibroblast growth factor 23 must be released (secreted) from the cell and it must attach (bind) to a receptor protein. To be secreted from the cell, sugar molecules are attached to fibroblast growth factor 23 by another protein called ppGalNacT3 in a process called glycosylation. Glycosylation allows fibroblast growth factor 23 to move out of the cell and protects the protein from being broken down. Once outside the bone cell, the protein must bind to a receptor protein called FGF receptor 1 that spans the membrane of kidney cells. Binding of fibroblast growth factor 23 to its receptor stimulates signaling that stops phosphate reabsorption into the bloodstream.

Studies suggest that fibroblast growth factor 23 has additional functions. It helps determine how much phosphate from the diet is absorbed by the intestines and plays a role in regulating vitamin D.

Fibroblast growth factor 23 is normally cut (cleaved) at a certain site, which turns off (inactivates) the protein. The cleavage site is located at positions 179 to 180 in the string of building blocks (amino acids) that make up the protein. This cleavage helps regulate the amount of active fibroblast growth factor 23 circulating in the bloodstream.

Health Conditions Related to Genetic Changes

hereditary hypophosphatemic rickets

At least three mutations in the *FGF23* gene have been found to cause a rare form of hereditary hypophosphatemic rickets known as autosomal dominant hypophosphatemic rickets. These mutations change single protein building blocks (amino acids) in fibroblast growth factor 23, which prevents the protein from being cleaved. As a result, the protein is not inactivated, and an increased amount of the full-length, active protein circulates in the bloodstream. Overactivity of fibroblast

growth factor 23 reduces phosphate reabsorption by the kidneys, leading to low levels of phosphate in the blood (hypophosphatemia) and related problems with bone growth in people with autosomal dominant hypophosphatemic rickets.

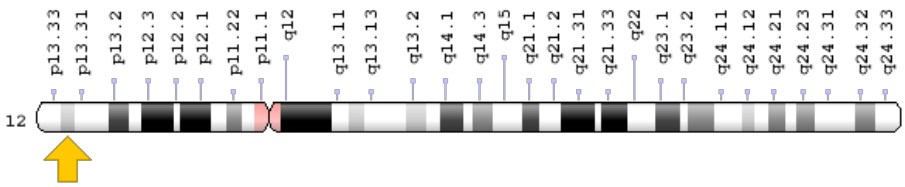
hyperphosphatemic familial tumoral calcinosis

At least seven mutations in the *FGF23* gene have been found to cause hyperphosphatemic familial tumoral calcinosis (HFTC), a condition characterized by an increase in the levels of phosphate in the blood (hyperphosphatemia) and abnormal deposits of phosphate and calcium (calcinosis) in the body's tissues. Mutations in the *FGF23* gene lead to the production of a protein with decreased function. This nonfunctional protein is quickly broken down in cells, leading to a shortage of available fibroblast growth factor 23. This protein shortage decreases signaling and increases the amount of phosphate that is reabsorbed back into the bloodstream by the kidneys, leading to hyperphosphatemia. Calcinosis results when the excess phosphate combines with calcium to form deposits that build up in soft tissues.

Chromosomal Location

Cytogenetic Location: 12p13.32, which is the short (p) arm of chromosome 12 at position 13.32

Molecular Location: base pairs 4,368,227 to 4,379,728 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ADHR
- FGF-23
- FGF23_HUMAN
- HPDR2
- HYPF
- phosphatonin

- PHPTC
- tumor-derived hypophosphatemia-inducing factor

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: Fibroblast Growth Factors
  https://www.ncbi.nlm.nih.gov/books/NBK6330/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28FGF23%5BTIAB%5D%29+OR+%28fibroblast+growth+factor+23%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- FIBROBLAST GROWTH FACTOR 23
  http://omim.org/entry/605380

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_FGF23.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=FGF23%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=3680
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/8074
- UniProt
  http://www.uniprot.org/uniprot/Q9GZV9

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